Remarks

In view of the above amendments and the following remarks, reconsideration of the outstanding office action is respectfully requested.

Claims 1, 7, 8, 11, 15, 16, 17, 20, 21, 23, 25, 28, 32, 33, 37, 42, 45, 49, 50, 53, 55, and 56 have been amended, and claims 4-6, 12-14, 29-31, 38-40, 46-48, and 54 have been cancelled without prejudice. The amendments to claims 1, 11, 20, 28, 37, 45, and 53 with respect to the listing of monoclonal antibodies is supported by the specification at page 7, page 16, and original claims 8, 16, 25, 33, 42, and 50, respectively. The additional amendments to claim 20 are inherent in the description of a myeloma patient to be treated in accordance with the present invention, and are intended to more particularly define the myeloma patient as one who is treated with polyclonal anti-thymocyte antiserum as opposed to another agent (e.g., chemotherapeutic agent). Other amended claims, such as claims 7, 8, 15-17, 21, 23, 25, 32, 33, 42, 49, 50, 55, and 56 have been amended to conform to preceding claims. Therefore, no new matter has been introduced by these amendments.

Claims 1-3, 7-11, 15-28, 32-37, 41-45, 49-53, 55, and 56 are pending and under examination.

Initially, applicant disputes the denial of the priority claim. The term rATG is one example of an anti-thymocyte antiserum (see page 27). Moreover, the use of several monoclonal antibodies is clearly described at pages 22, 27 (monoclonal antibodies against myeloma cells), 28 (monoclonal antibodies inducing activated B cell apoptosis). Although the claims of the provisional application recite the use of thymoglobulin, the description provided in the provisional application does describe work with a number of monoclonal antibodies.

The rejection of claims 45-52 under 35 U.S.C. § 112 (2nd para.) for indefiniteness is respectfully traversed in view of the above amendments. The method of treatment relates to treating an alloantibody disorder associated with transplantation (i.e., in a transplant recipient), and the body of the claim language has been amended to reflect this. The method is not for a transplant method *per se*. This rejection should therefore be withdrawn.

The rejection of claims 1-3, 9-11, 14, 16-20, 23, 25-28, 31-37, 40, 42-45, 48, and 50-56 under 35 U.S.C. § 112 (1st para.) for lack of an adequate written description is overcome by the above amendments deleting the term "variants". This rejection should be withdrawn.

The rejection of claims 1-3, 6-8, 10, 11, 14-17, 19, 20, 23-28, 31-37, 40-44, and 53-56 under 35 U.S.C. § 102(b) as anticipated by U.S. Patent Publication No. 2002/0197256 to Grewal ("Grewal"), as evidenced by Timm et al., "Thymoglobulin Targets Multiple Plasma Cell Antigens and has *In vitro* and *In vivo* Activity in Multiple Myeloma," *Leukemia: Official Journal of the Leukemia Society of America* 20(10):1863-1869 (2006) ("Timm"), is respectfully traversed.

Grewal describes the treatment of diseases characterized by cells that express CD40 using the combination of an agent that causes depletion of cells expressing CD40 and an agent that causes depletion of cells expressing CD20. Grewal reports in paragraph 147 (Figure 4) the treatment of multiple myeloma transplanted in SCID mice using anti-CD40 antibody in combination with anti-CD20 antibody. Timm is cited as evidence that multiple myeloma cells are CD138-positive.

With respect to claims 1, 11, 28, 37, 45, 53, and claims dependent thereon, because the claims have been amended to recite a particular set of cell surface markers, which does not include CD20 and CD40, the claims do not read on the method or compositions of Grewal.

With respect to claim 20 and claims dependent thereon, Grewal fails to teach or suggest an agent consisting of a polyclonal anti-thymocyte antiserum, which is not identical to the agents described by Grewal. Moreover, with respect to monoclonal antibodies, the recitation of a particular set of cell surface markers, which does not include CD20 and CD40, precludes this portion of the claim from reading on Grewal.

For these reasons, the rejection of claims 1-3, 6-8, 10, 11, 14-17, 19, 20, 23-28, 31-37, 40-44, and 53-56 as anticipated by Grewal is respectfully traversed.

The rejection of claims 1-4, 6, 8-10, 45, 46, 48, 50, 51, 53, 54, and 56 under 35 U.S.C. § 102(b) as anticipated by Bonnefoy-Berard et al., "Apoptosis Induced by Polyclonal Antilymphocyte Globulins in Human B-Cell Lines," *Blood* 83(4):1051-1059 (1994) ("Bonnefoy-Berard") is respectfully traversed.

Bonnefroy-Berard describes the composition of ATG and its ability to induce B cell apoptosis. However, Bonnefroy-Berard fails to teach or suggest that monoclonal antibodies, or binding fragments thereof, that are specific for any one or more CD27, CD30, CD32, CD38,

CD95, CD138, HLA-DR, HLA-A, HLA-B, and HLA-C would be useful in practicing the claimed invention. Therefore, this rejection is improper and should be withdrawn.

The rejection of claims 1-4, 6, 8, 10-12, 14, 16, 17, 19-21, 23, 25-27, 37, 38, 40, 42-46, 48, 50-54, and 56 under 35 U.S.C. § 102(b) as anticipated by Kröger et al., "Unrelated Stem Cell Transplantation in Multiple Myeloma After a Reduced-Intensity Conditioning with Pretransplantation Antithymocyte Globulin is Highly Effective with Low Transplantation-Related Mortality," *Blood* 100(12):3919-3924 (2002) ("Kröger"), as evidenced by Bonnefoy-Berard and Timm, is respectfully traversed.

The PTO asserts at page 6 of the office action that Kröger teaches the treatment of multiple myeloma with anti-thymoglobulin prior to stem cell transplantation. Applicants disagree with this assertion, because myeloma cells would have been destroyed by the prior pretreatment with fludarabine and melphalan employed in Kröger. Hence, the patient would not comprise myeloma cells at the time the anti-thymoglobulin was administered. In contrast to the use in the presently claimed invention, the use of anti-thymoglobulin in Kröger was simply to eliminate T cells before the transplantation. Because the myeloma cells were destroyed by the prior therapy, the myeloma cells could not have been bound by the antibodies in the anti-thymoglobulin antiserum.

With respect to claims 1, 11, 28, 37, 45, 53, and claims dependent thereon, because the claims have been amended to recite a particular set of cell surface markers, Kröger cannot anticipate these claims.

With respect to claim 20 and claims dependent thereon, Kröger fails to teach or suggest administering a polyclonal anti-thymocyte antiserum to a myeloma patient comprising myeloma cells for the reasons noted above. Moreover, with respect to monoclonal antibodies recited in claim 20, Kröger fails to teach or suggest this aspect of the invention.

For these reasons, the rejection of claims 1-4, 6, 8, 10-12, 14, 16, 17, 19-21, 23, 25-27, 37, 38, 40, 42-46, 48, 50-54, and 56 as anticipated by Kröger is improper and should be withdrawn.

The rejection of claims 1-8, 10, 45-48, 50-54, and 56 under 35 U.S.C. § 102(e) as anticipated by U.S. Patent Publication No. 2006/0147428 to Sachs ("Sachs") as evidenced by Bonnefoy-Berard is respectfully traversed.

Sachs teaches the administration of horse or other mammalian anti-human thymogloblulin prior to organ transplant or thymus replacement. Because Sachs fails to teach or suggest the use of monoclonal antibodies or binding fragments that bind to the cell surface markers recited in claims 1, 45, and 53, the rejection is improper and should be withdrawn.

The rejection of claims 1-4, 6-8, 10, 28, 29, 31, 33-36, 53, 54, and 56 under 35 U.S.C. § 102(e) as anticipated by U.S. Patent Publication No. 2006/0293391 to Birck et al. ("Birck"), as evidenced by Bonnefoy-Berard, is respectfully traversed. Birck recites the treatment of systemic lupus erythmatosus using deoxyspergualin in combination with anti-thymoglobulin. Because Birck fails to teach or suggest the use of monoclonal antibodies or binding fragments that bind to the cell surface markers recited in claims 1, 28, and 53, the rejection is improper and should be withdrawn.

The rejection of claims 1-3, 6-8, 10, 11, 14-17, 19, 20, 23-28, 31-37, 40-45, and 48-56 under 35 U.S.C. § 102(e) as anticipated by U.S. Patent Publication No. 2005/0070693 to Hansen et al. ("Hansen"), as evidenced by Timm, is respectfully traversed.

Hansen describes treating B cell malignancies and autoimmune diseases using anti-CD19 antibody. The teachings of Timm are noted above. The PTO asserts that Hansen further teaches the use of combinations of monoclonal antibodies.

With respect to claims 1, 11, 20, 28, 37, 45, and claims dependent thereon, applicants submit that that Hansen fails to teach or suggest the use of the recited monoclonal antibodies in the absence of an antibody for CD-19.

Moreover, with respect to claim 20 and the recited use of the "agent consisting of a polyclonal anti-thymocyte serum," applicants submit that Hansen fails to teach or suggest such a combination that constitutes the recited agent. Therefore, the rejection is improper and should be withdrawn.

The rejection of claims 1-6, 8-14, 16-23, 25-27, 37-40, 42-48, 50-54, and 56 under 35 U.S.C. § 103(a) for obviousness over Kröger as evidenced by Bonnefoy-Berard, in view of Sachs is respectfully traversed. As noted above, Kröger and Bonnefoy-Berard are both deficient in teaching or suggesting each and every limitation of the invention recited in claims 1, 11, 20, 37, 45, and 53. The PTO's reliance on Sachs for teaching anti-thymoglobulin obtained

from various mammals is irrelevant. Therefore, this rejection is improper and should be withdrawn.

The rejection of claims 1-6, 8-10, 28-31, 33-36, 45-48, 50-54, and 56 under 35 U.S.C. § 103(a) for obviousness over Birck, as evidenced by Bonnefoy-Berard, in view of Sachs is respectfully traversed. As noted above, Birck and Bonnefoy-Berard are both deficient in teaching or suggesting each and every limitation of the invention recited in claims 1, 28, 45, and 53. The PTO's reliance on Sachs for teaching anti-thymoglobulin obtained from various mammals is irrelevant. Therefore, this rejection is improper and should be withdrawn.

In view of all the foregoing, it is submitted that this case is in condition for allowance and such allowance is earnestly solicited.

Respectfully submitted,

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